REMARKS

Summary of Amendments

No claim has been amended. Claims 1-20 are in the application. Claims 12, 13 and 18-20 are withdrawn from consideration. Since no claim has been amended and no new claims have been added the listing of claims is unchanged from that which was submitted with the Reply to Restriction Requirement facsimile transmitted on August 10, 2005.

Claim Rejections-35 U.S.C. § 102 & 103

Claims 1-11 and 14-17 are rejected under 35 U.S.C. § 102(b) as being anticipated by each of Corbera et. al. (WO 99/05121), Atwal et. al. (WO 01/40231), Staveski et. al. (WO 01/56974) and Wong et. al. (US 5,416,087).

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the ... claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). Further more, a generic chemical formula will anticipate a claimed species covered by the formula when the species can be "at once envisaged" from the formula (see MPEP § 2131.02). "When the compound is not specifically named, but instead it is necessary to select portions of teachings within a reference and combine them, e.g., select various substituents from a list of alternatives given for placement at specific sites on a generic chemical formula to arrive at a specific composition, anticipation can only be found if the classes of substituents are sufficiently limited or well delineated. *Ex parte A*, 17 USPQ2d 1716 (Bd. Pat. App. & Inter. 1990). If one of ordinary skill in the art is able to "at once envisage" the specific compound within the generic chemical formula, the compound is anticipated. One of ordinary skill in the art must be able to draw the structural formula or write the name of each of the compounds included in the generic formula before any of the compounds can be "at once envisaged." One may look to the preferred embodiments to determine which compounds can be anticipated. *In re Petering*, 301 F.2d 676, 133 USPQ 275 (CCPA 1962)."

A. The 35 USC 102(b) rejection of compound claims 1-11:

The following is a quotation from MPEP § 2131.03:

If the claims are directed to a narrow range, the reference teaches a broad range, and there is evidence of unexpected results within the claimed narrow range, depending on the other facts of the case, it may be reasonable to conclude that the narrow range is not disclosed with "sufficient specificity" to constitute an anticipation of the claims. The unexpected results may also render the claims unobvious.

1. Corbera et. al. (WO 99/05121)

Corbera et. al. (WO 99/05121) relates to a group of structures represented by the specified general of formula (1), wherein X is either O or S, R1 is C1-C4 alkoxy or trifluoromethyl, and R2 is, *inter alia*, alkyl, cycloalkyl, heterocycloalkyl, aryl or arylalkyl. The genus represented by the formula (1) encompasses a vast number of compounds by virtue of, among others, the range of selections for R2. The breath of the general formula (1) is such that many choices must be made to arrive at the instantly claimed compounds. Additionally, specific examples of the generic formula (1) differ from the instantly claimed compounds. For example, the structure of the claimed chemical compounds differ from the specific compounds of the Corbera et. al. (WO 99/05121) with respect to the R1 variable group. The R1 variable group of the claimed compounds can be fluoren-9-one, isoxazole, cinnoline, isothiazole, isoquinoline, 9H-fluronene,1H-pyrazole or 9H-xanthene, all of which differ from the corresponding R2 group of the specific compounds in table 1 of Corbera et. al. (WO 99/05121). Furthermore, the instantly claimed compounds exhibit anti-tumor activity whereas the compounds in Corbera et. al. exhibit a sedative, anticonvulsive, hypnotic or general anesthesic activity. Corbera et. al. neither teaches nor suggest the anti-tumor activity. This difference in the activity of the claimed compounds and those of Corbera et. al. is significant in view of the fact that Corbera et. al. neither teach nor suggest that said structural difference would cause or result in the observed difference in biological activity. Without such teaching and/or suggestion one of ordinary skill in this art would not be motivated, on reading Corbera et. al. (WO 99/05121), to select and prepare the particular compounds defined in the rejected claims with reasonable expectation of

observing said anti-tumor activity. Therefore, one skilled in this art would neither, on reading Corbera et. al. (WO 99/05121), "at once envisage each member of" the general formula (1) [*In re Petering*, 301 F.2d 676, 133 USPQ 275 (CCPA 1962)] nor consider the claimed compounds described therein with "sufficient specificity" (see MPEP § 2131.03). Consequently, each and every element as set forth in the claim is not found "either expressly or inherently described" in Corbera et. al. (WO 99/05121). *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Therefore, the instantly claimed compounds are not described in the Corbera et. al. (WO 99/05121) within the meaning of the 35 USC 102(b). Therefore, the instantly claimed compounds are novel and patentable over Corbera et. al. (WO 99/05121).

2. Atwal et. al. (WO 01/40231)

Atwal et. al. (WO 01/40231) relates to a group heterocylic dihydropyrimidine structures represented by the general formula (I), wherein R1, R2, R3, R4, R5, X^1, X^2 and X^3 represent the variable substituents and ring members each of which has a range of selections. More particularly, the genus of the formula (I) describe pyrazolo[1,5-a]pyrimidines, which do not belong to the same class as the instantly claimed compounds. Moreover, the pyrazolo[1,5-a]pyrimidines of the formula (I) encompasses a vast number of compounds by virtue of the range of selections for the enumerated variable substiuent groups and ring members. Additionally, specific examples of the generic pyrazolo[1,5-a]pyrimidines formula (I) differ from the instantly claimed compounds. For example, the structure of the claimed chemical compounds differ from the specific compounds of the Atwal et. al. (WO 01/40231) with respect to the R1 variable group of the instantly claimed compounds. The R1 variable group of the claimed compounds can be fluoren-9-one, isoxazole, cinnoline, isothiazole, isoquinoline, 9H-fluronene,1H-pyrazole or 9H-xanthene whereas the corresponding variable substituent of the examples of piperazinyl containing compounds explicitly described in Atwal et. al. (WO 01/40231) is a 7-aryl-4,7-Dihydro-5-methylpyrazolo[1,5-a]pyrimindin-6-yl] radical. None of the alternatives for R1 variable group of the claimed chemical compounds is a 7-aryl-4,7-Dihydro-5-methylpyrazolo[1,5-a]pyrimindin-6-yl] radical. Furthermore, compounds in Atwal et. al. are inhibitors of potassium channel function (especially inhibitors of the K_v1 subfamily of voltage gated K^+ channels, more especially inhibitors $K_v1.5$ which has been linked to the ultra-rapidly

activating delayed rectifier K^+ current I_{Kur}) and are useful for the treatment of disorders such as arrhythmia and I_{Kur} –associated disorders. The instantly claimed compounds exhibit anti-tumor activity. Atwal et. al. neither teach or suggest the property of the anti-tumor activity of the instant compounds. This difference in the activity of the claimed compounds and those of Atwal et. al. is significant in view of the fact that Atwal et. al. neither teach nor suggest that said structural difference would cause or result in the observed difference in biological activity. Without such teaching and/or suggestion one of ordinary skill in this art would not be motivated, on reading Atwal et. al., to select and prepare the particular compounds defined in the rejected claims with reasonable expectation of observing said anti-tumor activity. The vast number of the pyrazolo[1,5-a]pyrimidines of the general formula (I), the absence of explicit examples falling witching the range of the instantly claimed compounds and the unexpected anti-tumor activity of the instant compounds all point to the one skilled in this art, on reading Atwal et. al. (WO 01/40231), would not receive sufficient guidance, teaching and/or suggestion to prepare the compounds of the instant invention with any reasonable expectation of observing the anti-tumor activity. One skilled in this art would neither, on reading Atwal et. al. (WO 01/40231), "at once envisage each member of" the general formula (1), [*In re Petering*, 301 F.2d 676, 133 USPQ 275 (CCPA 1962)], nor consider the instantly claimed compounds described therein with "sufficient specificity" (see MPEP § 2131.03). Consequently, each and every element as set forth in the claims are not found "either expressly or inherently described" in Atwal et. al. (WO 01/40231). *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Therefore, the instantly claimed compounds are novel and patentable over Atwal et. al. (WO 01/40231).

3. Staveski et. al. (WO 01/56974)

Staveski et. al. (WO 01/56974) relates to several classes of compounds represented by the generic formulae (I)-(V). Of these classes of compounds only those represented by generic formulae (I) and (IV) contain a piperazinyl ring. The generic formula (I) represents a group of indole carbonyl structures wherein R is hydrogen, alkyl, aryl, arylalkyl or hteroarylalkyl and Ra is a substituted or unsubstituted heterocyclic group. The class of indole carbonyl structures represented by the formula (I) encompasses a vast number of compounds and perhaps even an

infinite number of compounds since there is no express limit on the size of the alternatives for R (i.e. alkyl, aryl, arylalkyl or heteroarylalkyl) or the selection for Ra (i.e. substituted or unsubstituted heterocyclic). Specific examples the indole carbonyl structures represented by the generic formula (I), see tables 7-9, differ from the instantly claimed compounds. The R1 variable group of the claimed compounds is fluoren-9-one, isoxazole, cinnoline, isothiazole, isoquinoline, 9H-fluronene, 1H-pyrazole or 9H-xanthene whereas the corresponding group in the examples in tables 7-9 of Staveski et. al. (WO 01/56974) is an indolyl ring. Therefore, the examples of compounds in said tables are not identical to the instantly claimed compounds. The generic formula (IV) represents a group of biphenyl carbonyl structures wherein R_f and R_g are each, independently, substituted or unsubstituted alkyl, substituted or unsubstituted arylalkyl or substituted or unsubstituted heteroalkyl. The class of biphenyl carbonyl structures represented by the formula (IV) also encompasses a vast number of compounds and perhaps even an infinite number of compounds since there is no express limit on the size of the alternatives for R_f and R_g (i.e. substituted or unsubstituted alkyl, substituted or unsubstituted arylalkyl or substituted or unsubstituted heteroalkyl). Additionally, specific examples of the biphenyl carbonyl structures represented by the generic formula (IV), see table 4, differ from the instantly claimed compounds. The R1 variable group of the claimed compounds is fluoren-9-one, isoxazole, cinnoline, isothiazole, isoquinoline, 9H-fluronene, 1H-pyrazole or 9H-xanthene whereas the corresponding group in the examples in table 4 of Staveski et. al. (WO 01/56974) is a 1,1'-biphenyl radical. Therefore, the examples of compounds in said table are not identical to the instantly claimed compounds. Furthermore, the instantly claimed compounds exhibit anti-tumor activity. The compounds in Staveski et. al. are inhibitors of the Mycobacterial enoyl-ACP reductase required for cell wall biosynthesis and are useful for the treatment or prophylaxis of bacterial infections. Staveski et. al. neither teach nor suggest the anti-tumor property of the instant compounds. This difference in the activity of the claimed compounds and those of Staveski et. al. is significant in view of the fact that Staveski et. al. neither teach nor suggest that said structural difference would cause or result in the observed difference in biological activity. Without such teaching and/or suggestion one of ordinary skill in this art would not be motivated, on reading Staveski et. al., to select and prepare the particular compounds defined in the rejected claims with reasonable expectation of observing said anti-tumor activity. The vast number of the biphenyl carbonyl structures of generic formula (IV) or the indole carbonyl structures generic

formula (I), the absence of explicit examples of either classes of compounds falling witching the range of the instantly claimed compounds and the unexpected anti-tumor activity of the instant compounds all point to the fact that one skilled in this art, on reading Staveski et. al. (WO 01/56974), would not receive sufficient guidance, teaching and/or suggestion to prepare the compounds of the instant invention with any reasonable expectation of observing the anti-tumor activity. Consequently, each and every element as set forth in the claims are not found "either expressly or inherently described" in Staveski et. al. (WO 01/56974). *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Furthermore, one skilled in this art would neither, on reading Staveski et. al. WO 01/56974, "at once envisage each member of" the general formulae (I) or (IV), [*In re Petering*, 301 F.2d 676, 133 USPQ 275 (CCPA 1962)], nor consider the instantly claimed compounds described therein with "sufficient specificity"(see MPEP § 2131.03). Therefore, Staveski et. al. WO 01/56974 has not described to those with ordinary skill in this art each of the various permutations involved in arriving at the instantly claimed compounds as fully as if they had drawn each structural formula or had written each name. Hence, the instantly claimed compounds are novel and patentable over Staveski et. al. WO 01/56974.

4. Wong et. al. (US 5,416,087)

Wong et. al. (US 5,416,087) relates to bis-benzo cyclohepta piperidine, piperidylidene and piperazine compounds of the specified general formula (I), wherein T is nitrogen for the bis-benzo cyclohepta piperazine structures; Z is O or S; L is N or N^+O^-; and each of R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8 and R^9 has several alternatives. The bis-benzo cyclohepta piperazine structures represented by the formula (I) encompasses a vast number of compounds and perhaps even an infinite number of compounds since there is no express limit on the size of the alternatives for some of the variable groups. Additionally, specific examples of the bis-benzo cyclohepta piperazine structures represented by the generic formula (I), see tables 2 and 3, differ from the instantly claimed compounds. The R1 variable group of the claimed compounds is fluoren-9-one, isoxazole, cinnoline, isothiazole, isoquinoline, 9H-fluronene, 1H-pyrazole or 9H-xanthene whereas the corresponding group in the compounds number 7 and 8 in table 2 of said reference is a pyridinyl N-oxide moiety. Similarly, examples 5 and 8 in table 3 have piperazinyl compounds with the pyradinyl N-oxide moiety. Furthermore, the instantly claimed compounds exhibit anti-

tumor activity whereas the compounds of the cited art are PAF antagonists and antihistamines. This difference in the activity of the claimed compounds and those of Wong et. al. is significant in view of the fact that Wong et. al. neither teach nor suggest that said structural difference would cause or result in the observed difference in biological activity. Without such teaching and/or suggestion one of ordinary skill in this art would not be motivated, on reading Wong et. al. (US 5,416,087), to select and prepare the particular compounds defined in the rejected claims with reasonable expectation of observing said anti-tumor activity. The vast number of the benzo cyclohepta piperazine structures of generic formula (I), the absence of explicit examples of compounds falling within the range of the instantly claimed compounds and the unexpected anti-tumor activity of the instant compounds all point to the fact that one skilled in this art, on reading Wong et. al. (US 5,416,087), would not receive sufficient guidance, teaching and/or suggestion to prepare the compounds of the instant invention with any reasonable expectation of observing the anti-tumor activity. Consequently, each and every element as set forth in the claims is not found "either expressly or inherently described" in Wong et. al. (US 5,416,087). *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Furthermore, one skilled in this art would neither, on reading Wong et. al. (US 5,416,087), "at once envisage each member of" the general formula (I), [*In re Petering*, 301 F.2d 676, 133 USPQ 275 (CCPA 1962)], nor consider the instantly claimed compounds described therein with "sufficient specificity" (see MPEP § 2131.03). Therefore, the instantly claimed compounds are novel and patentable over Wong et. al. (US 5,416,087).

B. The 35 USC 102(b) rejection of the claims 14, 15, 16 and 17:

Claims 14 and 15 recite pharmaceutical composition that comprise at least one compound of the general formula (1) as recited in claim 1 of this application for a patent. The pharmaceutical compositions of these claims are not described, within the meaning of 35 U.S.C 102(b), by anyone of the references cited above since the compounds are structurally different and possess the unexpected anti-tumor activity which none of the cited are teach or suggest. As set forth supra, the instantly claimed compounds are novel and patentable over the cited prior art references. Consequently, pharmaceutical compositions of these novel compounds cannot be described by the cited references since they do not describe, teach or suggest the compounds in the first place. Therefore claims 14 and 15 are patentable over the cited references. Claims 16

and 17 are drawn respectively to the process of making said compositions and process of treating benign and malignant tumors. Based on the fact the instantly claimed compounds are novel, as shown supra, in view of the cited prior art references the process of making compositions thereof is also novel. The cited prior art references do not teach compounds with tumor activity of the instantly claimed compounds. Therefore the can neither anticipate the process of claim 17.

C. The 35 USC 103 rejection of the claims 1-11 and 14-17.

Claims 1-11 and 14-17 are rejected under 35 U.S.C. § 103(a) as being anticipated by each of Corbera et. al. (WO 99/05121), Atwal et. al. (WO 01/40231), Staveski et. al. (WO 01/56974) and Wong et. al. (US 5,416,087).

The instantly claimed compounds exhibit the unexpected property of the anti-tumor activity, which none of the cited prior art reference teach and/or suggest. Corbera et. al. (WO 99/05121) teach compounds that exhibit a sedative, anticonvulsive, hypnotic or general anesthesic activity. Atwal et. al. (WO 01/40231) teach compounds that are inhibitors of potassium channel function (especially inhibitors of the K_v1 subfamily of voltage gated K^+ channels, more especially inhibitors $K_v1.5$ which has been linked to the ultra-rapidly activating delayed rectifier K^+ current I_{Kur}) and are useful for the treatment of disorders such as arrhythmia and I_{Kur}–associated disorders. Staveski et. al. (WO 01/56974) teach compounds that are inhibitors of the Mycobacterial enoyl-ACP reductase required for cell wall biosynthesis and are useful for the treatment or prophylaxis of bacterial infections. Wong et. al. (US 5,416,087) teach compounds that are PAF antagonists and antihistamines. As shown supra, each reference describes a vast number of compounds and a different set of biological activity when compared to each other or to the anti-tumor activity of the instantly claimed compounds. This difference in the activity of the claimed compounds and the compounds of each of the cited reference is significant in view of the fact that none of them teach nor suggest the anti-tumor activity or the fact that the structural difference between the claimed compounds would cause or result in the observed difference in biological activity. Without such teaching and/or suggestion one of ordinary skill in this art would not, on reading anyone of the cited references, be motivated to select and prepare the particular compounds defined in the rejected claims with reasonable expectation of observing said anti-tumor activity. Therefore, the compounds of the instant invention are unobvious in

view of each of the prior art references cited above. Since the instantly claimed compounds are novel and unobvious in view of Corbera et. al. (WO 99/05121), Atwal et. al. (WO 01/40231), Staveski et. al. (WO 01/56974) or Wong et. al. (US 5,416,087), the pharmaceutical compositions containing them and the methods of treatment using them are also novel and unobvious in view of these references. Therefore, claims 14, 15, 17 are novel and patentable over these references. Claim 16 is drawn to making a pharmaceutical composition of the instantly claimed compounds. Based on the fact that the instantly claimed compounds are novel and exhibit anti-tumor activity, which is not taught or suggested by Corbera et. al. (WO 99/05121), Atwal et. al. (WO 01/40231), Staveski et. al. (WO 01/56974) or Wong et. al. (US 5,416,087), the process of making the compositions of the claimed compounds must necessarily be different and unobvious over said references. Therefore, claim 16 is novel, unobvious and patentable over Corbera et. al. (WO 99/05121), Atwal et. al. (WO 01/40231), Staveski et. al. (WO 01/56974) or Wong et. al. (US 5,416,087).

CONCLUSION

In view of the remarks and submission, the rejections of claims 1-11 and 14-17 are considered overcomed and withdrawal thereof, favorable consideration and allowance of all of the them are respectfully requested. Should the Examiner require or consider it advisable that the specification, claims and/or drawings be amended or corrected in formal respects in order to place the case in condition for allowance, then it is respectfully requested that such amendment or correction be carried out by Examiner's Amendment and the case passed to issue. Alternatively, should the Examiner feel that a personal discussion might be helpful in advancing this case to allowance, the Examiner is invited to telephone the undersigned.

The Commissioner is authorized to charge any required fees, including time extension fees, extra claim fees and any additional required fees, or credit any overpayment, to Goodwin Procter LLP Deposit Account No. 06-0923.

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